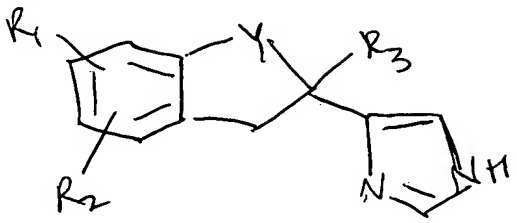
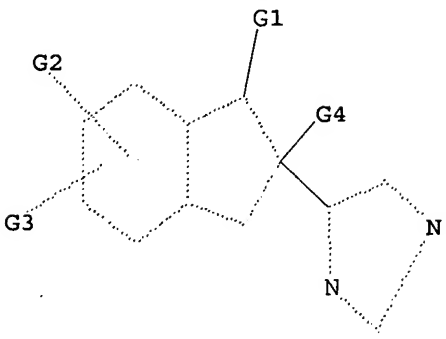
search for



10537177 process

L1 STR



G1 H,O

G2 OH,X

G3 H,X

G4 H,Ak,C

G5 A,C

Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 16:02:00 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -     9764 TO ITERATE

 20.5% PROCESSED     2000 ITERATIONS                                 1 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:       189358 TO   201202
PROJECTED ANSWERS:               1 TO      229

L2            1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:02:06 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   196289 TO ITERATE

100.0% PROCESSED   196289 ITERATIONS                              42 ANSWERS
SEARCH TIME: 00.00.04

L3           42 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              166.94     167.15

FILE 'CAPLUS' ENTERED AT 16:02:15 ON 20 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
```

Karen Cheng

10537177 process

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 19 Oct 2006 (20061019/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 16 L3

=> d ibib abs hitstr tot

Karen Cheng

Search of cmpd claimed

10537177

FILE 'REGISTRY' ENTERED AT 15:04:35 ON 20 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 19 OCT 2006 HIGHEST RN 910855-26-4
DICTIONARY FILE UPDATES: 19 OCT 2006 HIGHEST RN 910855-26-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

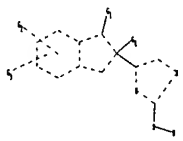
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

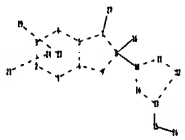
Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10537177d.str





chain nodes :
15 16 19 21 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14
chain bonds :
7-27 8-10 8-16 13-15 15-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-14 11-12 12-13 13-14

exact/norm bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-27 8-9 8-16 10-11 10-14 11-12
12-13 13-14 13-15

Karen Cheng

10537177

exact bonds :
8-10 15-26

G1:H,O

G2:OH,X

G3:H,X

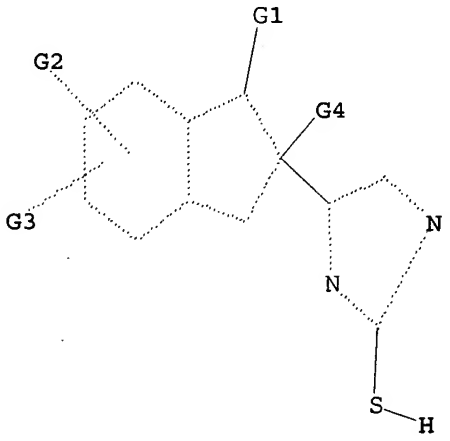
G4:H,Ak,C

G5:A,C

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 19:CLASS 21:CLASS
23:CLASS 24:CLASS 26:CLASS 27:CLASS

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,O

G2 OH,X

G3 H,X

G4 H,Ak,C

G5 A,C

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:05:07 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 776 TO ITERATE

Karen Cheng

10537177

100.0% PROCESSED 776 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 13849 TO 17191
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 15:05:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 16385 TO ITERATE

100.0% PROCESSED 16385 ITERATIONS 11 ANSWERS
SEARCH TIME: 00.00.01

L3 11 SEA SSS FUL L1

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'CAPLUS' ENTERED AT 15:05:18 ON 20 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 19 Oct 2006 (20061019/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 4 L3

=> d ibib abs hitstr tot

Karen Cheng

Date to beat: 1/8/2004

10537177

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

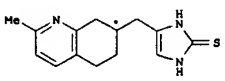
ACCESSION NUMBER: 2005:303397 CAPLUS
DOCUMENT NUMBER: 142:373839
TITLE: Preparation of 4-(2-methyl-5,6,7,8-tetrahydro-quinolin-7-ylmethyl)-1,3-dihydro-imidazole-2-thione as specific alpha2B adrenergic receptor agonist, and methods of using the same
INVENTOR(S): Heidelbaugh, Todd M.; Chow, Ken; Nguyen, Phong; Gil, Daniel; Donello, John E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 437,807.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005075366	A1	20050407	US 2004-950376	20040924
US 2004220402	A1	20041104	US 2003-437807	20030514
US 7091232	B2	20060815		
WO 2006036404	A1	20060406	WO 2005-US30158	20050822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2002-153328 B2 20020521
US 2003-437807 A2 20030514
US 2004-950376 A 20040924

OTHER SOURCE(S): MARPAT 142:373839
GI



I

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

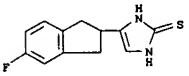
AB The compound of the formula (I) (wherein the * indicates an asym. carbon) and related 1,3-dihydro-imidazole-2-thione and 1,3-dihydro-imidazol-2-one compds. are prepared The compds. I is specific to alpha 2B adrenergic receptors in preference over alpha 2A and alpha 2C adrenergic receptors, and as such has no or only minimal cardiovascular and/or sedative activity. It is useful as medicament in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of alpha 2B adrenergic receptors. It is useful for alleviating pain, chronic pain, or allodynia and in particular useful for treating chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, neurodegenerative diseases, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammations, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. Thus, hydrogenation of quinaldine over PtO2 in CF3CO2H at 50 psi H pressure at room temperature for 1.5 h gave 98% 2-methyl-5,6,7,8-tetrahydroquinoline which was condensed with benzaldehyde in Ac2O at 155° for 4 h to give 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline (II). Ozonolysis of II with ozone in a mixture of CH2Cl2 and MeOH at -78° gave 50% 2-methyl-6,7-dihydro-5H-quinolin-8-one which was condensed with imidazole-4-carboxaldehyde in 40% aqueous H2SO4 at 110° for 12 h to give 98% 7-(1H-imidazol-4-ylmethylene)-2-methyl-6,7-dihydro-5H-quinolin-8-one (III). Hydrogenation of III over PtO2 in the presence of HClO4 in CF3CO2H at 50 psi H pressure at room temperature for 16 h gave 23% 7-(1H-imidazol-4-ylmethyl)-2-methyl-5,6,7,8-tetrahydroquinoline which was dissolved in a mixture of THF and H2O, treated with NaHCO3 and Ph chlorothioformate, and stirred at room temperature for 5 h to give 4-(2-methyl-5,6,7,8-tetrahydroquinolin-7-ylmethyl)-1,3-dihydroimidazole-2-thione (IV). The racemate IV was separated by preparative chiral HPLC with a CHIRALPAK-AD column and eluent hexane/ethanol(80/20) to give (+)-IV and (-)-IV. (-)-IV showed specific agonist activity on α2B adrenergic receptor at 92 nM but no activity on α1A and α2C receptors.

IT 628730-92-7P, 4-(5-Fluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-95-0P, 4-(5-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-96-1P, 4-(4-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-98-3P, 4-(5-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-99-4P, 4-(5-Chloro-4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-00-0P, 4-(4,5-Dichloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-02-2P, 4-(4-Iodoindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-10-2P, 4-(4-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-11-3P, 4-(4,6-Difluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-12-4P, 4-(4-Fluoro-6-methoxyindan-2-yl)-1,3-dihydroimidazole-2-thione

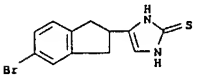
L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dihydroimidazolethiones and dihydroimidazolones as specific α2B adrenergic receptor agonists and therapeutic agents)

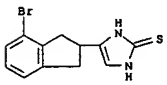
RN 628730-92-7 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-98-3 CAPLUS
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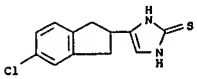

RN 628730-99-4 CAPLUS
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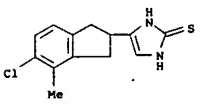
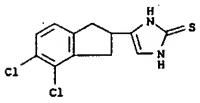
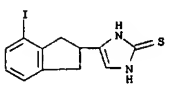


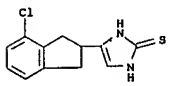
RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



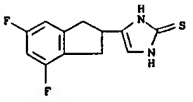
RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



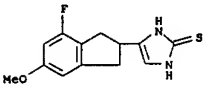
RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Karen Cheng

L4 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

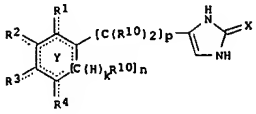


L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:934377 CAPLUS
DOCUMENT NUMBER: 141:395560
TITLE: Preparation of 4-(substituted cycloalkylmethyl)imidazole-2-thiones, 4-(substituted cycloalkenylmethyl)imidazole-2-thiones, 4-(substituted cycloalkylmethyl)imidazol-2-ones and 4-(substituted cycloalkenylmethyl)imidazol-2-ones and related compounds as agonists of alpha 2B adrenergic receptor
INVENTOR(S): Chow, Ken; Heidelbaugh, Todd; Gil, Daniel; Garst, Michael; Wheeler, Larry A.; Nguyen, Phong X.; Gomez, Dario G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 153,328, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004220402	A1	20041104	US 2003-437807	20030514
US 7091232	B2	20060815		
US 2005075366	A1	20050407	US 2004-950376	20040924
ZA 2004009333	A	20050519	ZA 2004-9333	20041119
US 2005267186	A1	20051201	US 2005-143334	20050602
US 2006148872	A1	20060706	US 2006-368990	20060306
US 2006149072	A1	20060706	US 2006-371612	20060309
PRIORITY APPLN. INFO.:			US 2002-153328	B2 20020521
			US 2003-437807	A2 20030514

OTHER SOURCE(S): MARPAT 141:395560
GI



I

AB The title compds. (I) [k = 0,1; n, p = 0-2; X = O, S; the dashed lines represent a bond, or absence of bond with the proviso that only one double bond is present in the ring and that two adjoining dashed lines do not both represent a bond; R1-R4 = H, (un)substituted Ph, C1-4 alkyl, C3-5 cycloalkyl, CH2CN, CH2SR5, CH2NR6R6, COR5, CH2OR5, OR6, SR6, NR6R6, C1-4

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

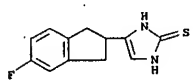
alkenyl, C1-4 alkynyl, C3-6 cycloalkyl, F, Cl, Br, iodo, CF3, cyano, an oxygen double bonded to the ring carbon with the proviso that the adjacent dashed line within the ring represents absence of a bond; R5 = H, OR7, C1-4 alkyl, CF3, C3-6 cycloalkyl, (un)substituted Ph, 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N, and 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R6 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted Ph, 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N, or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R7 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted phenyl; R10 = H, C1-6 alkyl] are prepd. The compds. I are specific or selective to α2B and/or α2C adrenergic receptors in preference over α2A adrenergic receptors, and the compds. I (X = O) also have the advantageous property that they have no or only minimal cardiovascular and/or sedative activity. The compds. I are useful as medicaments in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of α2B and/or α2C adrenergic receptors. The above diseases or conditions include chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammation, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. Thus, 1,2,3,4,5,6-hexahydro-pentalene-1-carboxaldehyde was treated with tosylmethyl isocyanide and NaCN in EtOH at room temp. for 20 min, concd., and heated with .apprx.7 M NH3/MeOH in a resealable tube at 100° for 15 h to give 4-(1,2,3,4,5,6-hexahydro-pentalen-1-ylmethyl)-1H-imidazole fumarate which was treated with NaHCO3 in THF at room temp. for 20 min and stirred with Ph chlorothioformate for 4 h to give 4-(1,2,3,4,5,6-hexahydro-pentalen-1-ylmethyl)-1,3-dihydroimidazole-2-thione (II). II acted as an agonist of α2B and α2C adrenergic receptor with EC50 of 5 and 110 nM, resp.

IT 628730-92-7P, 4-(5-Fluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-95-0P, 4-(5-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-96-1P, 4-(4-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-98-3P, 4-(5-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-99-4P, 4-(5-Chloro-4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-00-0P, 4-(4,5-Dichloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-02-2P, 4-(4-Iodoindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-10-2P, 4-(4-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-11-3P, 4-(4,6-Difluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-12-4P, 4-(4-Fluoro-6-methoxyindan-2-yl)-1,3-dihydroimidazole-2-thione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (cycloalkylmethyl)imidazolethiones,

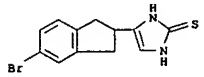
L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

(cycloalkenylmethyl)imidazolethiones, (cycloalkylmethyl)imidazolones and (cycloalkenylmethyl)imidazolones as agonists of α2B and/or α2C adrenergic receptor)

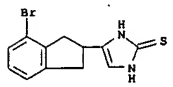
RN 628730-92-7 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



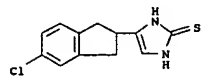
RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



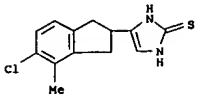
RN 628730-98-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



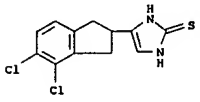
RN 628730-99-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-4-methyl-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Karen Cheng

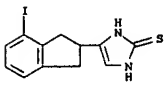
L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



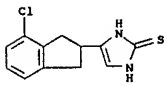
RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

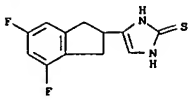


RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

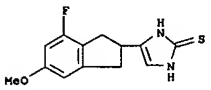


RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Applicant's

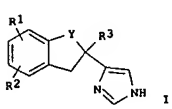
L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:606450 CAPLUS
DOCUMENT NUMBER: 141:140444
TITLE: Preparation of substituted imidazole derivatives
INVENTOR(S): Juujaervi, Paeivi; Parhi, Seppo; Karjalainen, Jaana
PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

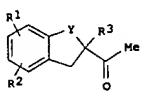
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063168	A1	20040729	WO 2004-FI4	20040108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
FI 2003000026	A	20040709	FI 2003-26	20030108
FI 116292	B1	20051031		
AU 2004203941	A1	20040729	AU 2004-203941	20040108
CA 2511969	AA	20040729	CA 2004-2511969	20040108
EP 1581504	A1	20051005	EP 2004-700707	20040108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004006676	A	20051220	BR 2004-6676	20040108
CN 1723202	A	20060118	CN 2004-80001979	20040108
JP 2006515349	T2	20060525	JP 2006-500148	20040108
US 2006025465	A1	20060202	US 2005-537177	20050601
NO 2005003712	A	20050801	NO 2005-3712	20050801

PRIORITY APPLN. INFO.: FI 2003-26 A 20030108
WO 2004-FI4 W 20040108

OTHER SOURCE(S): CASREACT 141:140444; MARPAT 141:140444
GI



I



II

AB Title compds. I (Y = CH2, CO; R1 = H, halo, OH; R2 = H, halo; R3 = H, alkyl) and their salts are prepared from ketones II. Thus, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole monohydrochloride was prepared in several steps from 2-acetyl-2-ethyl-5-fluoroindan.

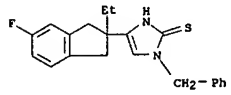
IT 727359-83-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted imidazole derivs.)

RN 727359-83-3 CAPLUS

Karen Cheng

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

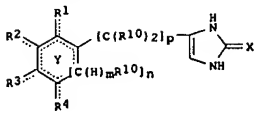
CN 2H-Imidazole-2-thione, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:951005 CAPLUS
DOCUMENT NUMBER: 140:5050
TITLE: Preparation of 4-substituted imidazole-2-thiones and imidazol-2-ones as agonists of alpha-2B and alpha-2C adrenergic receptors
INVENTOR(S): Chow, Ken; Heidelbaugh, Todd; Gil, Daniel; Garst, Michael; Wheeler, Larry A.; Nguyen, Phong X.; Gomez, Dario G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099795	A1	20031204	WO 2003-US15441	20030516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486537	AA	20031204	CA 2003-2486537	20030516
AU 2003245286	A1	20031212	AU 2003-245286	20030516
BR 2003011326	A	20050222	BR 2003-11326	20030516
EP 1507767	A1	20050223	EP 2003-738924	20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671671	A	20050921	CN 2003-817501	20030516
JP 2005531581	T2	20051020	JP 2004-507452	20030516
NO 2004005054	A	20050210	NO 2004-5054	20041119
ZA 2004009333	A	20050519	ZA 2004-9333	20041119
PRIORITY APPLN. INFO.:			US 2002-153328 A	20020521
			WO 2003-US15441 W	20030516

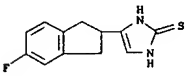
OTHER SOURCE(S): MARPAT 140:5050
GI



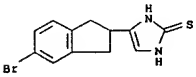
I

AB The title compds. [I; Y in the ring is optional and represents a heteroatom selected from N, O and S with the proviso that the N atom is trivalent, and the O or S atoms are divalent; m = 0, 1; n, p = 0, 1, 2; X = O, S; the dashed lines represent a bond, or absence of bond with the proviso that only one double bond is present in the ring and that two adjoining dashed lines do not both represent a bond; R1-R4 = independently H, (un)substituted Ph, C1-4 alkyl, C3-5 cycloalkyl, CH2CN, CH2SR5, CH2NR6R6, COR5, CH2OR5, OR6, SR6, NR6R6, C2-4 alkenyl or alkynyl, F, Cl, Br, iodo, CF3, cyano, an oxygen double bonded to the ring carbon with the proviso that the adjacent dashed line within the ring represents absence of a bond; R5 = H, OR7, C1-4 alkyl, CF3, C3-6 cycloalkyl, (un)substituted Ph or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R6 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted Ph or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R7 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted phenyl; R1 and R2 or R2 and R3 or R3 and R4 together can form a ring together with the resp. carbons to which each of these is attached; R10 = H, C1-6 or alkyl] are prepared These compds. possess specific or selective binding activity to α2B and/or α2C adrenergic receptors in preference over αA adrenergic receptors, and as such have no or only minimal cardiovascular and/or sedative activity. They are useful as medicaments in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of αB adrenergic receptors. The diseases and conditions include pain, allodynia, chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammations, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. For example, 4-(4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione showed agonism activity on α2B and α2C adrenergic receptors with EC50 of 3 and 13 nM, resp. and no

L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
activity on α2A adrenergic receptor.
IT 628730-92-7P 628730-95-0P 628730-96-1P
628730-98-3P 628730-99-4P 628731-00-0P
628731-02-2P 628731-10-2P 628731-11-3P
628731-12-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-substituted imidazolethiones and imidazolones as agonists of α2B and α2C adrenergic receptors)
RN 628730-92-7 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
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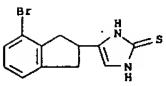
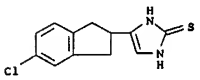
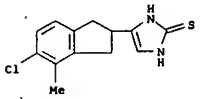


RN 628730-98-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

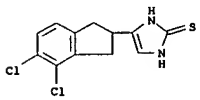
L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



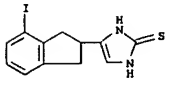
RN 628730-99-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-4-methyl-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

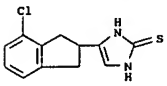


RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

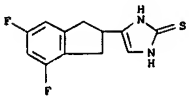


RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

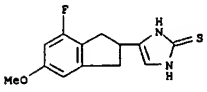
L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

10537177

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	20.90	188.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-3.00	-3.00

STN INTERNATIONAL LOGOFF AT 15:05:55 ON 20 OCT 2006

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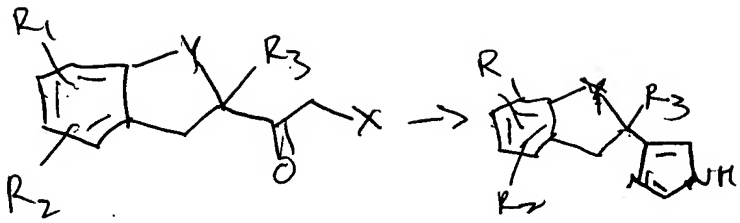
search rxn



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NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	AUG 09	INSPEC enhanced with 1898-1968 archive
NEWS 4	AUG 28	ADISCTI Reloaded and Enhanced
NEWS 5	AUG 30	CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 6	SEP 11	CA/CAplus enhanced with more pre-1907 records
NEWS 7	SEP 21	CA/CAplus fields enhanced with simultaneous left and right truncation
NEWS 8	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 9	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 10	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
NEWS 11	SEP 28	CEABA-VTB classification code fields reloaded with new classification scheme
NEWS 12	OCT 19	The Derwent World Patents Index suite of databases on STN will be enhanced and reloaded on October 22, 2006
NEWS 13	OCT 19	LOGOFF HOLD duration extended to 120 minutes
NEWS 14	OCT 19	E-mail format enhanced

NEWS EXPRESS	JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

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* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:33:14 ON 20 OCT 2006

=> fil casreact

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

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FILE 'CASREACT' ENTERED AT 15:33:27 ON 20 OCT 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT

FILE CONTENT:1840 - 15 Oct 2006 VOL 145 ISS 16

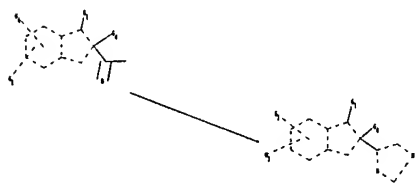
New CAS Information Use Policies, enter HELP USAGETERMS for details.

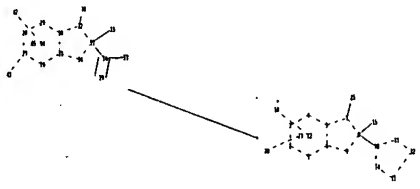
****
*
* CASREACT now has more than 10 million reactions
*
****

Some CASREACT records are derived from the ZIC/VINITI database (1974-1991) provided by InfoChem, INPI data prior to 1986, and Biotransformations database compiled under the direction of Professor Dr. Klaus Kieslich.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>
Uploading C:\Program Files\Stnexp\Queries\10537177rxn.str





chain nodes :
15 18 20 25 35 36 37 38 39 42 43
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 26 27 28 29 30 31 32 33 34
chain bonds :
7-25 8-10 8-15 32-38 33-35 33-36 36-37 36-39
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-14 11-12 12-13 13-14
26-27 26-31 27-28 28-29 29-30 30-31 30-32 31-34 32-33 33-34
exact/norm bonds :

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1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-25 8-9 8-15 10-11 10-14 11-12
12-13 13-14 26-27 26-31 27-28 28-29 29-30 30-31 30-32 31-34 32-33 32-38
33-34 33-35 36-39
exact bonds :
8-10 33-36 36-37

G1:H,O

G2:OH,X

G3:H,X

G4:H,Ak,C

G5:A,C

G6:H,OH,X

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 18:CLASS 20:CLASS 22:CLASS
23:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom 30:Atom 31:Atom 32:Atom
33:Atom 34:Atom 35:CLASS 36:CLASS 37:CLASS 38:CLASS 39:CLASS 42:CLASS
43:CLASS 44:CLASS 45:CLASS
fragments assigned product role:
containing 1
fragments assigned reactant/reagent role:
containing 26

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 15:34:28 FILE 'CASREACT'
SCREENING COMPLETE - 32 REACTIONS TO VERIFY FROM 11 DOCUMENTS

100.0% DONE 32 VERIFIED 0 HIT RXNS 0 DOCS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED VERIFICATIONS: 301 TO 979
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1 (0 REACTIONS)

=> s l1 full
FULL SEARCH INITIATED 15:34:32 FILE 'CASREACT'

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SCREENING COMPLETE - 1244 REACTIONS TO VERIFY FROM 193 DOCUMENTS

100.0% DONE 1244 VERIFIED 6 HIT RXNS 1 DOCS
SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1 (6 REACTIONS)

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	110.58	110.79

FILE 'CAPLUS' ENTERED AT 15:34:46 ON 20 OCT 2006
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FILE COVERS 1907 - 20 Oct 2006 VOL 145 ISS 18
FILE LAST UPDATED: 19 Oct 2006 (20061019/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 1 L3

=> d ibib abs hitstr 1

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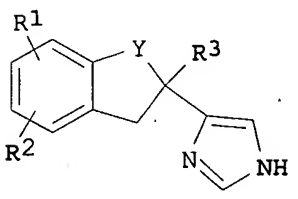
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:606450 CAPLUS
DOCUMENT NUMBER: 141:140444
TITLE: Preparation of substituted imidazole derivatives
INVENTOR(S): Juujaervi, Paeivi; Parhi, Seppo; Karjalainen, Jaana
PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063168	A1	20040729	WO 2004-FI4	20040108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
FI 2003000026	A	20040709	FI 2003-26	20030108
FI 116292	B1	20051031		
AU 2004203941	A1	20040729	AU 2004-203941	20040108
CA 2511969	AA	20040729	CA 2004-2511969	20040108
EP 1581504	A1	20051005	EP 2004-700707	20040108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004006676	A	20051220	BR 2004-6676	20040108
CN 1723202	A	20060118	CN 2004-80001979	20040108
JP 2006515349	T2	20060525	JP 2006-500148	20040108
US 2006025465	A1	20060202	US 2005-537177	20050601
NO 2005003712	A	20050801	NO 2005-3712	20050801

PRIORITY APPLN. INFO.: FI 2003-26 A 20030108
WO 2004-FI4 W 20040108

OTHER SOURCE(S): CASREACT 141:140444; MARPAT 141:140444
GI



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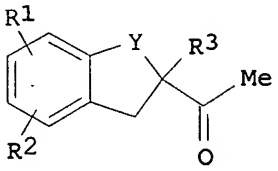

II

AB Title compds. I (Y = CH2, CO; R1 = H, halo, OH; R2 = H, halo; R3 = H, alkyl) and their salts are prepared from ketones II. Thus, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole monohydrochloride was prepared in several steps from 2-acetyl-2-ethyl-5-fluoroindan.

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=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	3.20	113.99

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

STN INTERNATIONAL LOGOFF AT 15:35:24 ON 20 OCT 2006

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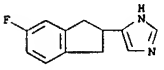
10537177 process Date bear = 1/8/04

L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:583318 CAPLUS
DOCUMENT NUMBER: 143:186200
TITLE: Lead Hopping Using SVM and 3D Pharmacophore Fingerprints
AUTHOR(S): Saeh, Jamal C.; Lyne, Paul D.; Takasaki, Bryan K.; Cosgrove, David A.
CORPORATE SOURCE: Cancer Discovery, AstraZeneca R&D Boston, Waltham, MA, 02451, USA
SOURCE: Journal of Chemical Information and Modeling (2005), 45(4), 1122-1133
CODEN: JCISD8; ISSN: 1549-9596
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The combination of 3D pharmacophore fingerprints and the support vector machine classification algorithm has been used to generate robust models that are able to classify compds. as active or inactive in a number of G-protein-coupled receptor assays. The models have been tested against progressively more challenging validation sets where steps are taken to ensure that compds. in the validation set are chemical and structurally distinct from the training set. In the most challenging example, we simulate a lead-hopping experiment by excluding an entire class of compds. (defined by a core substructure) from the training set. The left-out active compds. comprised approx. 40% of the actives. The model trained on the remaining compds. is able to recall 75% of the actives from the "new" lead series while correctly classifying >99% of the 5000 inactives included in the validation set.

IT 150586-64-4
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(lead hopping using SVM and 3D pharmacophore fingerprints)

RN 150586-64-4 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:303397 CAPLUS
DOCUMENT NUMBER: 142:373839
TITLE: Preparation of 4-(2-methyl-5,6,7,8-tetrahydro-quinolin-7-ylmethyl)-1,3-dihydro-imidazole-2-thione as specific alpha2B adrenergic receptor agonist, and methods of using the same
INVENTOR(S): Heidelbaugh, Todd M.; Chow, Ken; Nguyen, Phong; Gil, Daniel; Donello, John E.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 75 pp., Cont.-in-part of U.S. Ser. No. 437,807.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005075366	A1	20050407	US 2004-950376	20040924
US 2004220402	A1	20041104	US 2003-437807	20030514
US 7091232	B2	20060815		
WO 2006036404	A1	20060406	WO 2005-US30158	20050822

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:		
US 2002-153328	B2	20020521
US 2003-437807	A2	20030514
US 2004-950376	A	20040924

OTHER SOURCE(S): MARPAT 142:373839
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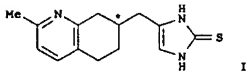
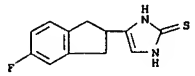


I

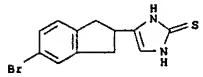
L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
AB The compound of the formula (I) (wherein the * indicates an asym. carbon) and related 1,3-dihydro-imidazole-2-thione and 1,3-dihydro-imidazol-2-one compds. are prepared The compds. I is specific to alpha 2B adrenergic receptors in preference over alpha 2A and alpha 2C adrenergic receptors, and as such has no or only minimal cardiovascular and/or sedative activity. It is useful as medicament in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of alpha 2B adrenergic receptors. It is useful for alleviating pain, chronic pain, or allodynia and in particular useful for treating chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, neurodegenerative diseases, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammations, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. Thus, hydrogenation of quinaldine over PtO2 in CF3CO2H at 50 psi H pressure at room temperature for 1.5 h gave 98% 2-methyl-5,6,7,8-tetrahydroquinoline which was condensed with benzaldehyde in Ac2O at 155° for 4 h to give 8-benzylidene-2-methyl-5,6,7,8-tetrahydroquinoline (II). Ozonolysis of II with ozone in a mixture of CH2Cl2 and MeOH at -78° gave 50% 2-methyl-6,7-dihydro-5H-quinolin-8-one which was condensed with imidazole-4-carboxaldehyde in 40% aqueous H2SO4 at 110° for 12 h to give 98% 7-(1H-imidazol-4-ylmethylene)-2-methyl-6,7-dihydro-5H-quinolin-8-one (III). Hydrogenation of III over PtO2 in the presence of HClO4 in CF3CO2H at 50 psi H pressure at room temperature for 16 h gave 23% 7-(1H-imidazol-4-ylmethyl)-2-methyl-5,6,7,8-tetrahydroquinoline which was dissolved in a mixture of THF and H2O, treated with NaHCO3 and Ph chlorothioformate, and stirred at room temperature for 5 h to give 4-(2-methyl-5,6,7,8-tetrahydroquinolin-7-ylmethyl)-1,3-dihydroimidazole-2-thione (IV). The racemate IV was separated by preparative chiral HPLC with a CHIRALPAK-AD column and eluent hexane/ethanol(80/20) to give (+)-IV and (-)-IV. (-)-IV showed specific agonist activity on α2B adrenergic receptor at 92 nM but no activity on α1A and α2C receptors.

IT 628730-92-7P, 4-(5-Fluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-95-0P, 4-(5-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-96-1P, 4-(4-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-98-3P, 4-(5-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-99-4P, 4-(5-Chloro-4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-00-0P, 4-(4,5-Dichloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-02-2P, 4-(4-Iodoindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-10-2P, 4-(4-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-11-3P, 4-(4,6-Difluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-12-4P, 4-(4-Fluoro-6-methoxyindan-2-yl)-1,3-dihydroimidazole-2-thione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of dihydroimidazolethiones and dihydroimidazolones as specific α2B adrenergic receptor agonists and therapeutic agents)

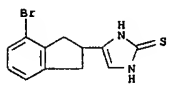
RN 628730-92-7 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



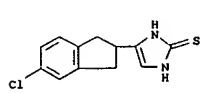
RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



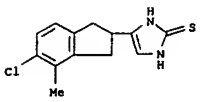
RN 628730-98-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



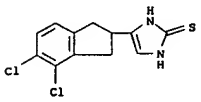
RN 628730-99-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-4-methyl-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

Karen Cheng

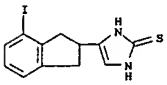
L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



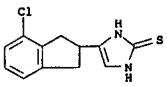
RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

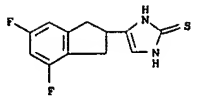


RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

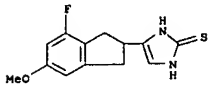


RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

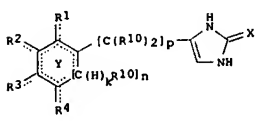


L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:934377 CAPLUS
DOCUMENT NUMBER: 141:395560
TITLE: Preparation of 4-(substituted cycloalkylmethyl)imidazole-2-thiones, 4-(substituted cycloalkenylmethyl)imidazole-2-thiones, 4-(substituted cycloalkylmethyl)imidazol-2-ones and 4-(substituted cycloalkenylmethyl)imidazol-2-ones and related compounds as agonists of alpha 2B adrenergic receptor
INVENTOR(S): Chow, Ken; Heidelbaugh, Todd; Gil, Daniel; Garst, Michael; Wheeler, Larry A.; Nguyen, Phong X.; Gomez, Dario G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No. 153,328, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004220402	A1	20041104	US 2003-437807	20030514
US 7091232	B2	20060815		
US 2005075366	A1	20050407	US 2004-950376	20040924
ZA 2004009333	A	20050519	ZA 2004-9333	20041119
US 2005267186	A1	20051201	US 2005-143334	20050602
US 2006148872	A1	20060706	US 2006-368990	20060306
US 2006149072	A1	20060706	US 2006-371612	20060309
PRIORITY APPLN. INFO.:			US 2002-153328	B2 20020521
			US 2003-437807	A2 20030514

OTHER SOURCE(S): MARPAT 141:395560
GI



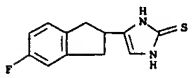
I

AB The title compds. (I) [k = 0,1; n, p = 0-2; X = O, S; the dashed lines represent a bond, or absence of bond with the proviso that only one double bond is present in the ring and that two adjoining dashed lines do not both represent a bond; R1-R4 = H, (un)substituted Ph, C1-4 alkyl, C3-5 cycloalkyl, CH2CN, CH2SR5, CH2NR6R6, COR5, CH2OR5, OR6, SR6, NR6R6, C1-4 alkenyl, C1-4 alkynyl, C3-6 cycloalkyl, F, Cl, Br, iodo, CF3, cyano, an oxygen double bonded to the ring carbon with the proviso that the adjacent dashed line within the ring represents absence of a bond; R5 = H, OR7, C1-4 alkyl, CF3, C3-6 cycloalkyl, (un)substituted Ph, 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N, and 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R6 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted Ph, 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N, or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R7 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted phenyl; R10 = H, C1-6 alkyl] are prepd. The compds. I are specific or selective to α2B and/or α2C adrenergic receptors in preference over α2A adrenergic receptors, and the compds. I (X = O) also have the advantageous property that they have no or only minimal cardiovascular and/or sedative activity. The compds. I are useful as medicaments in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of α2B and/or α2C adrenergic receptors. The above diseases or conditions include chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammation, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. Thus, 1,2,3,4,5,6-hexahydro-pentalene-1-carboxaldehyde was treated with tosylmethyl isocyanide and NaCN in EtOH at room temp. for 20 min, concd., and heated with .apprx.7 M NH3/MeOH in a resealable tube at 100° for 15 h to give 4-(1,2,3,4,5,6-hexahydro-pentalen-1-ylmethyl)-1H-imidazole fumarate which was treated with NaHCO3 in THF at room temp. for 20 min and stirred with Ph chlorothioformate for 4 h to give 4-(1,2,3,4,5,6-hexahydro-pentalen-1-ylmethyl)-1,3-dihydroimidazole-2-thione (II). II acted as an agonist of α2B and α2C adrenergic receptor with EC50 of 5 and 110 nM, resp.

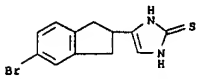
IT 628730-92-7P, 4-(5-Fluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-95-0P, 4-(5-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-96-1P, 4-(4-Bromoindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-98-3P, 4-(5-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628730-99-4P, 4-(5-Chloro-4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-00-0P, 4-(4,5-Dichloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-02-2P, 4-(4-Iodoindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-10-2P, 4-(4-Chloroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-11-3P, 4-(4,6-Difluoroindan-2-yl)-1,3-dihydroimidazole-2-thione 628731-12-4P, 4-(4-Fluoro-6-methoxyindan-2-yl)-1,3-dihydroimidazole-2-thione
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (cycloalkylmethyl)imidazolethiones, (cycloalkylmethyl)imidazolones and (cycloalkenylmethyl)imidazolones as agonists of α2B and/or α2C adrenergic receptor)

RN 628730-92-7 CAPLUS

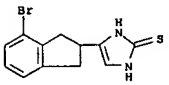
L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2H-Imidazole-2-thione,
4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)



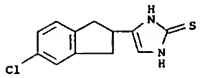
RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)

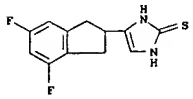


RN 628730-98-3 CAPLUS
CN 2H-Imidazole-2-thione,
4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)

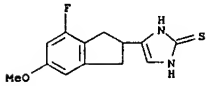


RN 628730-99-4 CAPLUS
CN 2H-Imidazole-2-thione,
4-(5-chloro-2,3-dihydro-4-methyl-1H-inden-2-yl)-1,3-
dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

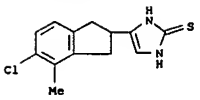


RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-
1,3-dihydro- (9CI) (CA INDEX NAME)

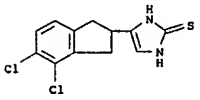


REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

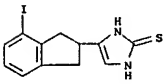
L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



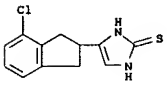
RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-
dihydro- (9CI) (CA INDEX NAME)



RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)



RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione,
4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-
(9CI) (CA INDEX NAME)

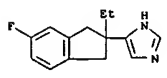


RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-
dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:872679 CAPLUS
DOCUMENT NUMBER: 141:343519
TITLE: Treatment of epilepsy
INVENTOR(S): Haapalinna, Antti; Pitkaenen, Asla
PATENT ASSIGNEE(S): Orion Corporation, Finland
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004089349	A2	20041021	WO 2004-FI220	20040408
WO 2004089349	A3	20041209		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2521656	AA	20041021	CA 2004-2521656	20040408
EP 1610771	A2	20060104	EP 2004-726526	20040408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
JP 2006522777	T2	20061005	JP 2006-505635	20040408
PRIORITY APPLN. INFO.:			US 2003-461413P	P 20030410
			WO 2004-FI220	W 20040408

AB The disclosure relates to a method for the inhibition of the development of epilepsy with an alpha2-adrenoceptor antagonist or a pharmaceutically acceptable salt or ester thereof.
IT 150586-58-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α2-adrenoceptor antagonists for treatment of epilepsy)
RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



10537177 process

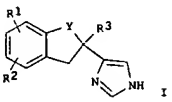
Applicant

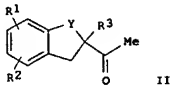
L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:606450 CAPLUS
DOCUMENT NUMBER: 141:140444
TITLE: Preparation of substituted imidazole derivatives
INVENTOR(S): Juujaervi, Paeivi; Parhi, Seppo; Karjalainen, Jaana
PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004063168	A1	20040729	WO 2004-FI4	20040108
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ				
FI 2003000026	A	20040709	FI 2003-26	20030108
FI 116292	B1	20051031		
AU 2004203941	A1	20040729	AU 2004-203941	20040108
CA 2511969	AA	20040729	CA 2004-2511969	20040108
EP 1581504	A1	20051005	EP 2004-700707	20040108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2004006676	A	20051220	BR 2004-6676	20040108
CN 1723202	A	20060118	CN 2004-80001979	20040108
JP 2006515349	T2	20060525	JP 2006-500148	20040108
US 2006025465	A1	20060202	US 2005-537177	20050601
NO 2005003712	A	20050801	NO 2005-3712	20050801

PRIORITY APPLN. INFO.:
FI 2003-26 A 20030108
WO 2004-FI4 W 20040108

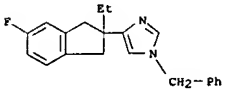
OTHER SOURCE(S): CASREACT 141:140444; MARPAT 141:140444
GI


I

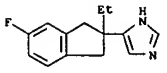

II

AB Title compds. I (Y = CH2, CO; R1 = H, halo, OH; R2 = H, halo; R3 = H, alkyl) and their salts are prepared from ketones II. Thus, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole monohydrochloride was prepared in several steps from 2-acetyl-2-ethyl-5-fluoroindan.
IT 150586-58-6P

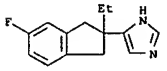
L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(phenylmethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of substituted imidazole derivs.)
RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

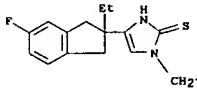


IT 150586-72-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of substituted imidazole derivs.)
RN 150586-72-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT 727359-83-3P 727359-84-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted imidazole derivs.)
RN 727359-83-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro-1-(phenylmethyl)- (9CI) (CA INDEX NAME)



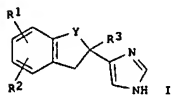
RN 727359-84-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1-

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:430735 CAPLUS
DOCUMENT NUMBER: 141:12273
TITLE: Improved fast-dispersing formulations containing substituted imidazole derivatives
INVENTOR(S): Banbury, Susan; Juujarvi, Paivi; Grother, Leon P.; Lunsmann, Walter; Murray, Owen; Savola, Juha-Matti
PATENT ASSIGNEE(S): R.P. Scherer Technologies, Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043439	A1	20040527	WO 2003-US34934	20031103
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR				
CA 2503630	AA	20040527	CA 2003-2503630	20031103
AU 2003287476	A1	20040603	AU 2003-287476	20031103
EP 1581192	A1	20051005	EP 2003-781716	20031103
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2006517516	T2	20060727	JP 2004-551671	20031103
NO 2005002360	A	20050606	NO 2005-2360	20050512
US 2006134194	A1	20060622	US 2005-534117	20051006

PRIORITY APPLN. INFO.:
GB 2002-26076 A 20021108
WO 2003-US34934 W 20031103

OTHER SOURCE(S): MARPAT 141:12273
GI


I

AB The present invention provides a fast- dispersing, solid dosage form containing, as an active ingredient, a substituted imidazole derivative of general formula (I), wherein Y is -CH2- or -CO-; R1 is H, halo or hydroxy; R2 is H or halo; and R3 is H or lower alkyl (e.g. C1 to C4 alkyl, preferably C1 or C2 alkyl), or a pharmaceutically acceptable salt, such as an acid addition

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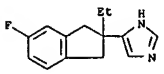
10537177 process

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
salt, e.g. the hydrochloride, of a compd. of the general formula, so as to
promote pre-gastric absorption of the active ingredient.
IT 150586-58-6, Fipamezole
RL: PAC (Pharmacological activity); BIOL (Biological study)
(improved fast-dispersing formulations containing substituted imidazole
derivs.)
RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

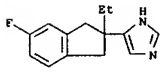
L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:412807 CAPLUS
DOCUMENT NUMBER: 140:395558
TITLE: Oromucosal formulation and process for preparing the same
INVENTOR(S): Savola, Juha-Matti; Juujaervi, Paeivi; Ilkka, Jukka
PATENT ASSIGNEE(S): Oy Juvantia Pharma Ltd., Finland
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004041271	A1	20040521	WO 2003-FI850	20031110
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2505139	AA	20040521	CA 2003-2505139	20031110
AU 2003276317	A1	20040607	AU 2003-276317	20031110
EP 1560581	A1	20050810	EP 2003-810489	20031110
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003016071	A	20050927	BR 2003-16071	20031110
CN 1711083	A	20051221	CN 2003-80102885	20031110
JP 2006506411	T2	20060223	JP 2004-549237	20031110
US 2006052429	A1	20060309	US 2005-534091	20050506
NO 2005002752	A	20050607	NO 2005-2752	20050607

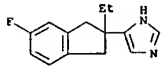
PRIORITY APPLN. INFO.: FI 2002-2007 A 20021108
WO 2003-FI850 W 20031110

OTHER SOURCE(S): MARPAT 140:395558
AB An oromucosal formulation comprises as an active ingredient an indenylimidazole derivative or an acid addition salt thereof, preferably 4-(ethyl-5-fluoroindan-2-yl)-1H-imidazole (fipamezole), together with additives conventionally used in oromucosal formulations. The formulations are effective and easy to handle, and therefore they have an advantage in terms of practical administration to the patient. For example, an oral spray contained fipamezole 15, methylparaben 1.8, propylparaben 0.2, aspartame 0.5, black currant 502.009A 0.4 mg, ethanol 0.416 mL, and purified water q.s. to 1 mL.
IT 150586-58-6, Fipamezole 150586-72-4
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oromucosal formulations of fipamezole)

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



RN 150586-72-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



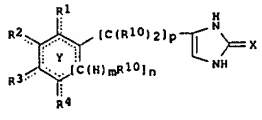
● HCl

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:951005 CAPLUS
DOCUMENT NUMBER: 140:5050
TITLE: Preparation of 4-substituted imidazole-2-thiones and imidazol-2-ones as agonists of alpha-2B and alpha-2C adrenergic receptors
INVENTOR(S): Chow, Ken; Heidelbaugh, Todd; Gil, Daniel; Garst, Michael; Wheeler, Larry A.; Nguyen, Phong X.; Gomez, Dario G.
PATENT ASSIGNEE(S): Allergan, Inc., USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099795	A1	20031204	WO 2003-US15441	20030516
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2486537	AA	20031204	CA 2003-2486537	20030516
AU 2003245286	A1	20031212	AU 2003-245286	20030516
BR 2003011326	A	20050222	BR 2003-11326	20030516
EP 1507767	A1	20050223	EP 2003-738924	20030516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1671671	A	20050921	CN 2003-817501	20030516
JP 2005531581	T2	20051020	JP 2004-507452	20030516
NO 2004005054	A	20050210	NO 2004-5054	20041119
ZA 2004009333	A	20050519	ZA 2004-9333	20041119

PRIORITY APPLN. INFO.: US 2002-153328 A 20020521
WO 2003-US15441 W 20030516

OTHER SOURCE(S): MARPAT 140:5050
GI



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Cmpd 7
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10537177 process

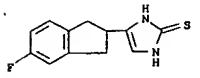
L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

AB The title compds. [I: Y in the ring is optional and represents a heteroatom selected from N, O and S with the proviso that the N atom is trivalent, and the O or S atoms are divalent; m = 0, 1; n, p = 0, 1, 2; X = O, S; the dashed lines represent a bond, or absence of bond with the proviso that only one double bond is present in the ring and that two adjoining dashed lines do not both represent a bond; R1-R4 = independently H, (un)substituted Ph, C1-4 alkyl, C3-5 cycloalkyl, CH2CN, CH2SR5, CH2NR6R6, COR5, CH2OR5, OR6, SR6, NR6R6, C2-4 alkenyl or alkynyl, F, Cl, Br, iodo, CF3, cyano, an oxygen double bonded to the ring carbon with the proviso that the adjacent dashed line within the ring represents absence of a bond; R5 = H, OR7, C1-4 alkyl, CF3, C3-6 cycloalkyl, (un)substituted Ph or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R6 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted Ph or 5 or 6 membered heteroaryl having 1 to 3 heteroatoms selected from O, S, and N; R7 = H, C1-4 alkyl, allyl, C3-6 cycloalkyl, (un)substituted phenyl; R1 and R2 or R2 and R3 or R3 and R4 together can form a ring together with the resp. carbons to which each of these is attached; R10 = H, C1-6 or alkyl] are prepared These compds. possess specific or selective binding activity to α2B and/or α2C adrenergic receptors in preference over αA adrenergic receptors, and as such have no or only minimal cardiovascular and/or sedative activity. They are useful as medicaments in mammals, including humans, for treatment of diseases and or alleviation of conditions which are responsive to treatment by agonists of αB adrenergic receptors. The diseases and conditions include pain, allodynia, chronic pain, visceral pain, neuropathic pain, corneal pain, glaucoma, elevated intraocular pressure, ischemic neuropathies, neurodegenerative diseases, diarrhea, nasal congestion, muscle spasticity, diuresis, withdrawal syndromes, optic neuropathy, spinal ischemia, stroke, memory and cognition deficits, attention deficit disorder, psychoses, manic disorders, anxiety, depression, hypertension, congestive heart failure, cardiac ischemia, arthritis, spondylitis, gouty arthritis, osteoarthritis, juvenile arthritis, autoimmune diseases, lupus erythematosus, chronic gastrointestinal inflammations, Crohn's disease, gastritis, irritable bowel disease (IBD), functional dyspepsia and ulcerative colitis. For example, 4-(4-methylindan-2-yl)-1,3-dihydroimidazole-2-thione showed agonism activity on α2B and α2C adrenergic receptors with EC50 of 3 and 13 nM, resp. and no activity on α2A adrenergic receptor.

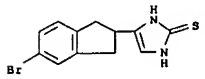
IT 628730-92-7P 628730-95-0P 628730-96-1P
628730-98-3P 628730-99-4P 628731-00-0P
628731-02-2P 628731-10-2P 628731-11-3P
628731-12-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-substituted imidazolethiones and imidazolones as agonists of α2B and α2C adrenergic receptors)

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

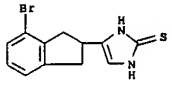
RN 628730-92-7 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



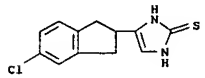
RN 628730-95-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628730-96-1 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-bromo-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

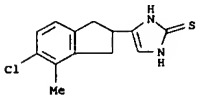


RN 628730-98-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

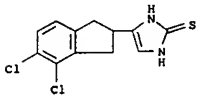


RN 628730-99-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(5-chloro-2,3-dihydro-4-methyl-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

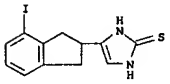
L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



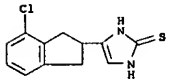
RN 628731-00-0 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,5-dichloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



RN 628731-02-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(2,3-dihydro-4-iodo-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

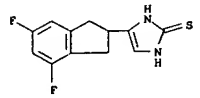


RN 628731-10-2 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

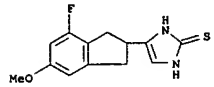


RN 628731-11-3 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4,6-difluoro-2,3-dihydro-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 628731-12-4 CAPLUS
CN 2H-Imidazole-2-thione, 4-(4-fluoro-2,3-dihydro-6-methoxy-1H-inden-2-yl)-1,3-dihydro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

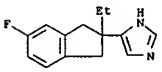
Karen Cheng

10537177 process

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:796479 CAPLUS
DOCUMENT NUMBER: 139:286371
TITLE: α2-Adrenoceptor antagonists for the treatment of pyychostimulant dependence and dependence-related withdrawal symptoms
INVENTOR(S): Haapalinna, Antti; Viitamaa, Timo; Virtanen, Raimo
PATENT ASSIGNEE(S): Orion Corporation, Finland
SOURCE: PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

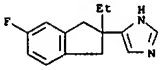
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003082275	A1	20031009	WO 2003-FI240	20030328
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003216954	A1	20031013	AU 2003-216954	20030328
US 2006058364	A1	20060316	US 2005-509152	20051014
PRIORITY APPLN. INFO.:			US 2002-368165P	P 20020329
			WO 2003-FI240	W 20030328

AB The invention provides a method for treatment of dependence and dependence-related withdrawal symptoms caused by the discontinuation of subacute or chronic use of psychostimulant agents, to ease a patient's withdrawal from the psychostimulants with an α2-adrenoceptor antagonist (e.g. atipamezole), or a pharmaceutically acceptable ester or salt thereof.
IT 150586-58-6, MPV 1730 150586-72-4, MPV 1730 hydrochloride
RL: PAC (Pharmacological activity); BIOL (Biological study)
(α2-adrenoceptor antagonists for treatment of pyychostimulant dependence and dependence-related withdrawal symptoms)
RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 150586-72-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



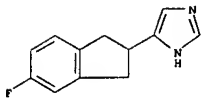
● HCl

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:416430 CAPLUS
DOCUMENT NUMBER: 139:332942
TITLE: Identification and characterization of the imidazoline I2b-binding sites in the hamster brown adipose tissue as a study model for imidazoline receptors
AUTHOR(S): Romer, L.; Wurster, S.; Savola, J.-M.; Raasmaja, A.
CORPORATE SOURCE: Preclinical Research, Orion Pharma, Orion Corporation, Turku, Finland
SOURCE: Archives of Physiology and Biochemistry (2003), 111(2), 159-166
CODEN: APBIF5; ISSN: 1381-3455
PUBLISHER: Swets & Zeitlinger B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The imidazoline-type compound, MPV-1743, has been found to activate non-shivering thermogenesis (NST) in brown adipose tissue (BAT) of the genetically obese Zucker rats. The regulation of NST in BAT is linked to the catecholamine metabolism, and the imidazoline I2-binding sites have been found on the monoamine oxidase, a catecholamine metabolizing enzyme. In this study, the I2-binding sites of hamster BAT have been characterized using a receptor binding assay with 3H-idazoxan as a radioligand, and the interaction of MPV-1743 with these I2-binding sites has been studied using the enantiomers of MPV 1743, i.e., MPV 2088 and MPV 2089. Cirazoline was used to determine the specific binding of 3H-idazoxan to the imidazoline I2-binding sites. Rauwolscine was added in the 3H-idazoxan binding assay in order to inhibit any binding to potential α2-adrenergic sites. In the presence of rauwolscine mask 3H-Idazoxan labeled a population of non-adrenergic binding sites expressing the properties of the imidazoline I2b-receptor subtype similar to that found in the rat liver (cirazoline >> guanabenz = amiloride >> clonidine). The binding of 3H-idazoxan to the I2b-binding sites could be displaced by the imidazole compds. with the following affinities: detomidine (KiHigh 9.2 nM; KiLow 3200 nM), MPV-2088 (KiHigh 19 nM; KiLow 760 nM) and MPV-2089 (KiHigh 190 nM; KiLow 1300 nM), atipamezole (3500 nM) and dexmedetomidine (Ki 8400 nM). These results have shown that the hamster BAT contains the imidazoline I2b-binding sites with heterogeneous binding properties for some test compds. In addition, the enantiomers of MPV 1743, i.e., MPV 2088 and MPV 2089, had high affinity to these BAT imidazoline I2b-binding sites. Therefore, it is suggested that the regulation of NST in the hamster BAT may be an attractive model to study the role of imidazoline I2b-binding sites.
IT 163112-34-3, MPV 2088 163112-37-6, MPV 2089
RL: PAC (Pharmacological activity); BIOL (Biological study)
(identification and characterization of imidazoline I2b-binding sites in hamster brown adipose tissue)
RN 163112-34-3 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

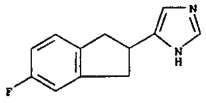
L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

RN 163112-37-6 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



● HCl

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

Karen Cheng

10537177 process

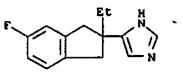
L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:287959 CAPLUS
DOCUMENT NUMBER: 139:316253
TITLE: Fipamezole hydrochloride: antiparkinsonian α2-adrenoceptor antagonist
AUTHOR(S): Sorbera, L. A.; Castaner, J.; Bayes, M.
CORPORATE SOURCE: Prous Science, Barcelona, 08080, Spain
SOURCE: Drugs of the Future (2003), 28(1), 14-17
CODEN: DRFUD4; ISSN: 0377-8282
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Dopaminergic agents, particularly levodopa and direct or indirect dopamine agonists, are the mainstay of treatment for Parkinson's disease. However, while treatment with these agents is effective in the early phases of the disease, the benefits decrease with disease progression and problems such as dyskinesia and on-off phenomenon begin to manifest. An interesting therapeutic strategy that has recently drawn attention is increasing (nor)adrenergic tone by blocking presynaptic α2-adrenoceptors. This mechanism could be effective against dyskinesia, including levodopa-induced dyskinesia and related movement disorders. Fipamezole hydrochloride is one such novel α2-adrenoceptor antagonist that exhibits potent antagonism against all human α2-adrenoceptor subtypes. The agent has shown excellent preclin. activity and was chosen for further development as a treatment for Parkinson's disease with emphasis on dyskinesia and related movement disorders. The agent is currently undergoing phase II development for the treatment of Parkinson's disease.

IT 150586-72-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of fipamezole hydrochloride for treatment of Parkinson's disease)

RN 150586-72-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

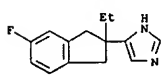
ACCESSION NUMBER: 2002:391506 CAPLUS
DOCUMENT NUMBER: 136:380121
TITLE: α2-Adrenoceptor antagonists for the prevention of development of dyskinesias
INVENTOR(S): Haapalinna, Antti; Juhila, Juuso; Sirvio, Jouni
PATENT ASSIGNEE(S): Orion Corporation, Finland
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002039991	A2	20020523	WO 2001-FI989	20011113
WO 2002039991	A3	20020829		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2428603	AA	20020523	CA 2001-2428603	20011113
AU 2002023703	A5	20020527	AU 2002-23703	20011113
EP 1333828	A2	20030813	EP 2001-996370	20011113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004513917	T2	20040513	JP 2002-542366	20011113
US 2002115703	A1	20020822	US 2001-987382	20011114
US 2004039041	A1	20040226	US 2003-416721	20030909
PRIORITY APPLN. INFO.:			US 2000-248004P P	20001114
			WO 2001-FI989 W	20011113

AB The invention relates to the prevention of the development of sensitization caused by chronic use of dopaminergic agents using an α2-adrenoceptor antagonist, e.g. atipamezole, or a pharmaceutically acceptable ester or salt thereof.

IT 150586-58-6
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α2-adrenoceptor antagonist for prevention of development of sensitization from chronic use of dopaminergic agent)

RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



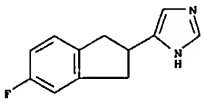
L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Karen Cheng

10537177 process

L4 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:350095 CAPLUS
DOCUMENT NUMBER: 129:90794
TITLE: Protean Agonism at α2A-Adrenoceptors
AUTHOR(S): Jansson, Christian C.; Kukkonen, Jyrki P.; Nasman, Johnny; Huifang, Ge; Wurster, Siegfried; Virtanen, Raimo; Savola, Juha-Matti; Cockcroft, Vic; Akerman, E.
O.
CORPORATE SOURCE: Department of Biochemistry and Pharmacy, Abo Akademi University, Turku, Finland
SOURCE: Molecular Pharmacology (1998), 53(5), 963-968
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The coupling of the endogenously expressed α2A-adrenoceptors in human erythroleukemia cells (HEL 92.1.7) to Ca2+ mobilization and inhibition of forskolin-stimulated cAMP production was investigated. The two enantiomers of medetomidine [(±)-[4-(1-[2,3-dimethylphenyl]ethyl)-1H-imidazole]HCl] produced opposite responses. Dexmedetomidine behaved as an agonist in both assays (i.e., it caused Ca2+ mobilization and depressed forskolin-stimulated cAMP production). Levome-detomidine, which is a weak agonist in some test systems, reduced intracellular Ca2+ levels and further increased forskolin-stimulated cAMP production and therefore can be classified as an inverse agonist. A neutral ligand, MPV-2088, antagonized responses to both ligands. Several other, chemical diverse α2-adrenergic ligands also were tested. Ligands that could promote increases in Ca2+ levels and inhibition of cAMP production could be classified as full or partial agonists. Their effects could be blocked by the α2-adrenoceptor antagonist rauwolscine and by pertussis toxin treatment. Some typical antagonists such as rauwolscine, idazoxan, and atipamezole had inverse agonist activity like levomedetomidine. The results suggest that the α2A-adrenoceptors in HEL 92.1.7 cells exist in a precoupled state with pertussis toxin-sensitive G proteins, resulting in a constitutive mobilization of intracellular Ca2+ and inhibition of cAMP production in the absence of agonist. This constitutive activity can be antagonized by inverse agonists such as levomedetomidine and rauwolscine. Levomedetomidine can be termed a "protean agonist" because it is capable of activating uncoupled α2-adrenoceptors in other systems and inhibiting the constitutive activity of precoupled α2-adrenoceptors in HEL 92.1.7 cells. With this class of compds., the inherent receptor "tone" could be adjusted, which should provide a new therapeutic principle in receptor dysfunction.
IT 163112-34-3, MPV 2088
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(protean agonism at α2A-adrenoceptors)
RN 163112-34-3 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

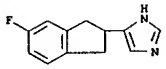


● HCl

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:346343 CAPLUS
DOCUMENT NUMBER: 127:75825
TITLE: Anti-obesity effect of MPV-1743 AIII, a novel imidazoline derivative, in genetic obesity
AUTHOR(S): Savontaus, Erika; Raasmaja, Atso; Rouru, Juha; Koulu, Markku; Pesonen, Ullamari; Virtanen, Raimo; Savola, Juha-Matti; Huupponen, Risto
CORPORATE SOURCE: Department of Pharmacology and Clinical Pharmacology, University of Turku, Kiinamyllynkatu 10, Turku, FIN-20520, Finland
SOURCE: European Journal of Pharmacology (1997), 328(2/3), 207-215
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB MPV-1743 AIII ((±)-4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole) is a novel imidazoline derivative In this study, it was shown to bind with high affinity to α2-adrenoceptor subtypes α2A (IC50 = 0.66±0.06 nM), α2B (IC50 = 3.8±0.53 nM), α2C (IC50 = 3.1±0.61 nM) in the recombinant S115 cells and to α2D (IC50 = 0.94±0.10 nM) in the rat submandibular gland. MPV-1743 AIII also showed remarkably high affinity to α1-adrenoceptors (IC50 = 150±12 nM) in the rat cerebral cortex and to imidazoline I2b-binding sites (IC50 = 150±5.0 nM) in the rat liver. The functional α2-adrenoceptor antagonistic effect of MPV-1743 AIII was demonstrated by studying the ability of orally administered MPV-1743 AIII to reverse and prevent the α2-adrenoceptor agonist detomidine-induced mydriasis in rat. The anti-obesity effect of MPV-1743 AIII was investigated in genetically obese (fa/fa) Zucker rats in two different phases of obesity. Chronic treatment with MPV-1743 AIII (0.3-3 mg/kg per day p.o. for 3 wk) dose dependently decreased weight gain in early-phase obesity. In fully established obesity, GDP binding to mitochondria and expression of uncoupling protein mRNA were increased in brown adipose tissue by MPV-1743 AIII indicating an activation of non-shivering thermogenesis. The present study shows that MPV-1743 AIII has a modest anti-obesity effect in the genetic rodent model of obesity. The relative importance of α2- and α1-adrenoceptors and imidazoline I2b-binding sites in mediating the effects of MPV-1743 AIII needs further evaluation.
IT 150586-64-4, MPV 1743AIII
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(imidazoline derivative MPV-1743 AIII antiobesity effect in genetic obesity: adrenergic and imidazoline receptor mediation)
RN 150586-64-4 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Karen Cheng

10537177 process

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:557222 CAPLUS
DOCUMENT NUMBER: 122:290853
TITLE: Preparation of enantiomers of 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole
INVENTOR(S): Karjalainen, Arto Johannes; Virtanen, Raimo Einari; Karjalainen, Arja Leena; Parhi, Seppo Sulevi Lennart; Eloranta, Maire Marjatta; Haapalinna, Antti Sakari
PATENT ASSIGNEE(S): Orion-Yhtymae OY, Finland
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9500492	A1	19950105	WO 1994-FI263	19940616
W: AT, AU, BG, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KR, KZ, LU, LV, NL, NO, NZ, PL, PT, RO, RU, SE, SI, SK, TJ, UA, US, UZ				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2165459	AA	19950105	CA 1994-2165459	19940616
AU 9469725	A1	19950117	AU 1994-69725	19940616
EP 703903	A1	19960403	EP 1994-918395	19940616
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1125439	A	19960626	CN 1994-192476	19940616
JP 08511554	T2	19961203	JP 1994-502468	19940616
ZA 9404346	A	19950215	ZA 1994-4346	19940617
LT 3468	B	19951025	LT 1994-1959	19940617
NO 9505056	A	19951213	NO 1995-5056	19951213
FI 9506040	A	19951215	FI 1995-6040	19951215
LV 11462	B	19961220	LV 1995-376	19951219
PRIORITY APPLN. INFO.:			GB 1993-12669 A	19930618
			WO 1994-FI263 W	19940616

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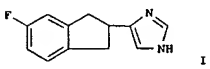
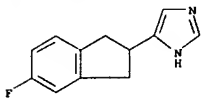


I

AB Optical isomers of the title compds. and pharmaceutically acceptable salts thereof, potent in the treatment of cognitive disorders, are prepared. To

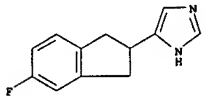
L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

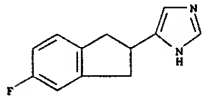
RN 163112-35-4 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



RN 163112-37-6 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride, (+)- (9CI) (CA INDEX NAME)

Rotation (+).



● HCl

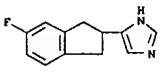
IT 163112-33-2P 163112-36-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of enantiomers of (fluorodihydroindenyl)imidazole)
RN 163112-33-2 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, (-)-, (S-(R*,R*))-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 163112-32-1

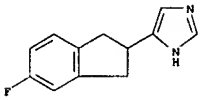
Karen Cheng

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
H2SO4 were added 4-(2,3-dihydro-1H-inden-2-yl)-1H-imidazole-HCl and urea nitrate to give 4-(2,3-dihydro-5-nitro-1H-inden-2-yl)-1H-imidazole which was reduced to the amino deriv. and converted to the title compd. (±-I)converted into diastereoisomer salts, and sepg. the mixt. by fractional crystn. and converting the sepd. enantiomer to the free base. Biol. activity was demonstrated.
IT 150586-64-4P 163112-32-1P 163112-34-3P
163112-35-4P 163112-37-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of enantiomers of (fluorodihydroindenyl)imidazole)
RN 150586-64-4 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



RN 163112-32-1 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

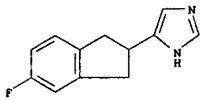


RN 163112-34-3 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CMF C12 H11 F N2

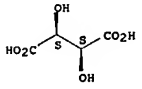
Rotation (-).



CM 2

CRN 147-71-7
CMF C4 H6 O6

Absolute stereochemistry.

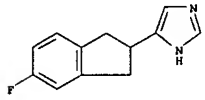


RN 163112-36-5 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, (+)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 163112-35-4
CMF C12 H11 F N2

Rotation (+).



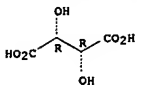
CM 2

CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.

10537177 process

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:625954 CAPLUS
DOCUMENT NUMBER: 119:225954
TITLE: Preparation of substituted imidazole derivatives as adrenoceptor antagonists
INVENTOR(S): Karjalainen, Arto Johannes; Virtanen, Raimo Einari; Karjalainen, Arja Leena; Eloranta, Maire Marjatta; Salonen, Jarmo Sakari; Sipila, Hannu Tapani; Haapalinna, Antti Sakari
PATENT ASSIGNEE(S): Orion-Yhtyma Oy, Finland
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

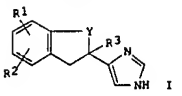
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9313074	A1	19930708	WO 1992-FI349	19921218
W: AT, AU, BG, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KR, LU, NL, NO, NZ, PL, PT, RO, RU, SE, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9331605	A1	19930728	AU 1993-31605	19921218
AU 664584	B2	19951123		
EP 618906	A1	19941012	EP 1993-900200	19921218
EP 618906	B1	19980422		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 67548	A2	19950428	HU 1994-1823	19921218
HU 220043	B	20011028		
JP 07506087	T2	19950706	JP 1993-511460	19921218
JP 3276371	B2	20020422		
PL 172532	B1	19971031	PL 1992-304150	19921218
AT 165350	E	19980515	AT 1993-900200	19921218
ES 2115046	T3	19980616	ES 1993-900200	19921218
RU 2120440	C1	19981020	RU 1994-31215	19921218
CA 2117305	C	20031125	CA 1992-2117305	19921218
FI 9402882	A	19940616	FI 1994-2882	19940616
FI 104968	B1	20000515		
NO 9402335	A	19940620	NO 1994-2335	19940617
NO 304227	B1	19981116		
US 5498623	A	19960312	US 1994-244932	19940919

PRIORITY APPLN. INFO.: GB 1991-27050 A 19911220
WO 1992-FI349 A 19921218

OTHER SOURCE(S): MARPAT 119:225954
GI

patent 4,689,339

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

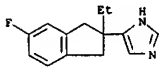


I

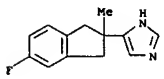
AB Title compds. I [Y = CH2, CO; R1 = F, Cl, OH; R2 = H, F, Cl; R3 = H, Me, Et], excluding 4-(5-chloro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole and 4-(4-chloro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole] and their salts are prepared Their peroral bioavailability is good. These compds. are especially useful in the treatment of cognitive disorders. Thus, nitration of 4-(2-ethyl-2,3-dihydro-1H-inden-2-yl)-1H-imidazole with urea nitrate followed by PtO2 catalyzed hydrogenation and fluoboric acid fluorination gave 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-1H-imidazole (II). ED50 of II 15 μg/kg\, i.v..

IT 150586-58-6P 150586-59-7P 150586-60-0P
150586-61-1P 150586-62-2P 150586-63-3P
150586-64-4P 150586-65-5P 150586-66-6P
150586-67-7P 150586-68-8P 150586-72-4P
150586-75-7P 150586-76-8P 150586-80-4P
150586-83-7P 150586-87-1P 150586-90-6P
150586-93-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and adrenoceptor antagonistic activity of)

RN 150586-58-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

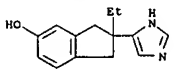


RN 150586-59-7 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-2-methyl-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

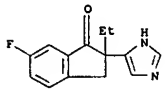


RN 150586-60-0 CAPLUS
CN 1H-Inden-5-ol, 2-ethyl-2,3-dihydro-2-(1H-imidazol-4-yl)- (9CI) (CA INDEX NAME)

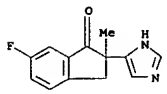
L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



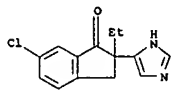
RN 150586-61-1 CAPLUS
CN 1H-Inden-1-one, 2-ethyl-6-fluoro-2,3-dihydro-2-(1H-imidazol-4-yl)- (9CI) (CA INDEX NAME)



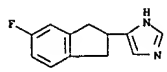
RN 150586-62-2 CAPLUS
CN 1H-Inden-1-one, 6-fluoro-2,3-dihydro-2-(1H-imidazol-4-yl)-2-methyl- (9CI) (CA INDEX NAME)



RN 150586-63-3 CAPLUS
CN 1H-Inden-1-one, 6-chloro-2-ethyl-2,3-dihydro-2-(1H-imidazol-4-yl)- (9CI) (CA INDEX NAME)

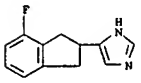


RN 150586-64-4 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

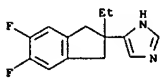


Karen Cheng

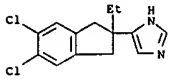
L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 150586-65-5 CAPLUS
CN 1H-Imidazole, 4-(4-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



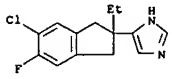
RN 150586-66-6 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5,6-difluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



RN 150586-67-7 CAPLUS
CN 1H-Imidazole, 4-(5,6-dichloro-2-ethyl-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

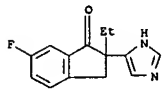


RN 150586-68-8 CAPLUS
CN 1H-Imidazole, 4-(5-chloro-2-ethyl-6-fluoro-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



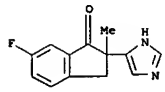
RN 150586-72-4 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



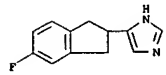
● HCl

RN 150586-83-7 CAPLUS
CN 1H-Inden-1-one, 6-fluoro-2,3-dihydro-2-(1H-imidazol-4-yl)-2-methyl-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

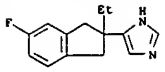
RN 150586-87-1 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

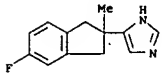
RN 150586-90-6 CAPLUS
CN 1H-Imidazole, 4-(4-fluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



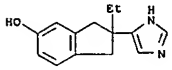
● HCl

RN 150586-75-7 CAPLUS
CN 1H-Imidazole, 4-(5-fluoro-2,3-dihydro-2-methyl-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

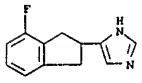
RN 150586-76-8 CAPLUS
CN 1H-Inden-5-ol, 2-ethyl-2,3-dihydro-2-(1H-imidazol-4-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

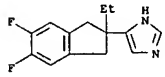
RN 150586-80-4 CAPLUS
CN 1H-Inden-1-one, 2-ethyl-6-fluoro-2,3-dihydro-2-(1H-imidazol-4-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



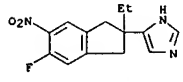
● HCl

RN 150586-93-9 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5,6-difluoro-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)

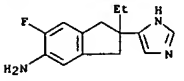


● HCl

IT 150586-91-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and catalytic hydrogenation of, in preparation of antagonistic adrenoceptor)
RN 150586-91-7 CAPLUS
CN 1H-Imidazole, 4-(2-ethyl-5-fluoro-2,3-dihydro-6-nitro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

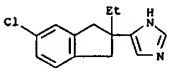


IT 150586-92-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and fluorination of, in preparation of antagonistic adrenoceptor)
RN 150586-92-8 CAPLUS
CN 1H-Inden-5-amine, 2-ethyl-6-fluoro-2,3-dihydro-2-(1H-imidazol-4-yl)- (9CI)
(CA INDEX NAME)

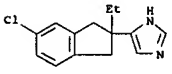


IT 150586-94-0P 150586-95-1P 150586-96-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of antagonistic adrenoceptor)

RN 150586-94-0 CAPLUS
CN 1H-Imidazole, 4-(5-chloro-2-ethyl-2,3-dihydro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

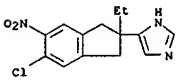


RN 150586-95-1 CAPLUS
CN 1H-Imidazole, 4-(6-chloro-2-ethyl-2,3-dihydro-1H-inden-2-yl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 150586-96-2 CAPLUS
CN 1H-Imidazole, 4-(5-chloro-2-ethyl-2,3-dihydro-6-nitro-1H-inden-2-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

10537177 process

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	82.68	249.83

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-12.00	-12.00

STN INTERNATIONAL LOGOFF AT 16:03:13 ON 20 OCT 2006

Karen Cheng